Al-Mustansiriyah Journal of Science
ISSN: 1814-635X (print), ISSN: 2521-3520 (online)
Volume 28, Issue 1, 2017
DOI: http: //doi.org/10.23851/mjs.v28i1.310

Research Article

A Comparative Study between C-Reactive Protein and Procalcitonin in Iraqi Burn Patients

Alia E. Al-Ubadi[1], Abbas B. Al-Bahadly[2], Meroj A. Jasem[1], Intesar Y. Salman[3]
[1] Department of Biology, College of Science, Mustansiriyah University, IRAQ.
[2] Ministry of Health, IRAQ.
[3] Kidney Transplant Center, Ministry of Health, IRAQ.
*Correspondant email: aliaalubadi65@yahoo.com

ArticleInfo

Received
2/11/2016

Accepted
12/12/2016

Abstract

Association between Procalcitonin (PCT) and C-reactive protein (CRP) and burn injury was evaluated in 80 burned patients from Al-Kindy and Imam Ali hospitals in Baghdad-Iraq. Patients were divided into two groups, survivor group 56 (70%) and non-survivor group 24 (30%). PCT was estimated using (Human Procalcitonin ELISA kit) provided by RayBio/USA while CRP was performed using a latex agglutination kit from Chromatest (Spain).

Our results declared that the mean of Total Body Surface Area (TBSA %) affected were 63.5% range (36%–95%) in non-survivor patients, while 26.5% range (10%–70%) in survivor patients. There is a significant difference between the two groups (P = 0.00), the higher mean percentage of TBSA has a significant association with mortality.

Serum PCT and CRP were measured at the three times of sampling (within the first 48hr following admission, after 5thdays and after 10th days). The mean of PCT serum concentrations in non-survivor group (2638 ± 3013pg/ml) were higher than that of survivor group (588 ± 364pg/ml). Significantly high levels of CRP were found between the survivor and non-survivor groups especially in the 10th day of admission P=0.000, present study show that significant differences is found within the non-survivor group through the three times P= 0.01, while results were near to significant differences within survivor group through the three times (P= 0.05).

Keywords: Procalcitonin, C-reactive protein, Biomarkers, Burned patients.

الخلاصة

درست علاقة البروكالسيتونين (Procalcitonin (PCT والبروتين الفعال سي (C-reactive protein CRP) في 80 مريض من مرضى الحروق الذين أدخلوا الى كل من مستشفى الكندي العام التعليمي ومستشفى الإمام علي العام في بغداد - العراق للفترة ما بين تشرين الاول /2015 و شباط/2016. قسم المرضى إلى مجموعتين، مجموعة الناجين 56 (70٪) ومجموعة غير الناجين (الموتى) 24 (30٪). تم قياس البروكالسيتونين بتقنية الامتزاز المناعي المقترن بالانزيم باستخدام عدة مختبرية والمجهزة من قبل شركة RayBio الأمريكية في حين تم قياس البروتين الفعال سي (CRP باستخدام عدة اللاتكس من شركة Chromatest /الاسبانية.

اوضحت الدراسة ان النسبة المئوية للمساحة السطحية للحروق Total Body Surface Area (TBSA%) كانت 63.5٪ وتتراوح ما بين (36٪-95٪) في مجموعة غير الناجين، بينما كانت في مجموعة الناجين 26.5٪ (10٪ -70٪)، اذ لوحظ وجود ارتفاع معنوي عالي بين المجموعتين P = 0.000، وارتفاع النسبة المئوية للمساحة السطحية للحروق له علاقة وثيقة مع وفاة مرضى الحروق.

تم قياس التركيز المصلي للبروكالسيتونين (PCT والبروتين الفعال سي في الأوقات الثلاثة من أخذ العينات، خلال 48 الساعة الأولى من دخول المستشفى، وبعد اليوم الخامس واليوم العاشر من دخول المستشفى ، كان متوسط التركيز للبروكالسيتونين في مجموعة غير الناجين (2638 ± 3013 بيكوغرام /مل) أعلى من تركيزه في مجموعة الناجين (588 ± 364 بيكوغرام /مل). بينما كانت مستويات البروتين الفعا سي (CRP) عالية في مجموعةغير الناجين مقارنة مع مجموعة الناجين، لا سيما في اليوم العاشر من الدخول للمستشفى P = 0. 000، اذ لوحظ ارتفاعا معنويا عاليا في مجموعة غير الناجين للأوقات الثلاثة P = 0.01 و قريبة من المعنوية في مجموعة الناجين للأوقات الثلاثة P = 0.05.

Introduction

Burns injuries are a prevalent and hard critical care problem. The necessities of specific skills converge on stabilizing the patient, avoiding infection, and enhancing functional recovery [1]. Important progress being made in burn patient

care, but we still need for comprehension of inflammatory and anti-inflammatory systems (schemes) and their interactions in states of burned patients provides new opportunities to more accurately diagnosis, including progressing wound healing, grafts healing, controlling inflammation and efficiency of treatment [2].

There are many typical inflammatory markers related to the existence of certain infections like Leucocyte count, Erythrocyte Sedimentation Rate (ESR) and C-reactive protein (CRP), which remain elevated in burn patients but their increase or decrease are not always dependable[3].

((The kinetics of C-reactive protein is slower than that of the PCT, and C-reactive protein concentrations are induced near to their maximum during less severe symptoms of systemic inflammation and organ dysfunction))[4].

The level of PCT in the circulation system of healthy people is lower than (0.01 µg/L) and it increases in a reaction of proinflammatory of bacterial infection. The PCT has been widely tested for diagnosis and suiTable use as antibiotic therapy in both children and adults for different infectious diseases in various researches in different countries [5-7]. The PCT has been studied as biomarker to assist diagnosis and aid prognostication in bacterial infections and sepsis [4][8-11].

This study was conducted in an attempt to prove the efficiency of plasma PCT level as a critical biomarker to detect infection and even death in burned patients.

Material and Methodologies

Eighty (80) burned patients were included in this study they were admitted to the burn emergency department at Al-kindy and Imam Ali hospitals in Baghdad, Iraq from the period from October/2015 until February/2016. The patients, including were with signs of burn injuries within two days of admission. Patients were only recruited in daytime, as the time between sample collection and laboratory analysis was less than six hours.

Clinical Investigation

The PCT was estimated using (Human Procalcitonin ELISA kit) provided by RayBio/USA which is an *in vitro* enzyme-linked immunosorbent assay for the quantitative measurement of human Procalcitonin in serum with normal range <0.5 ng/ml according to the manufacturer's specifications, while CRP was performed using latex agglutination kit from Chromatest (Spain).

Statistical Analysis

Data generated from this work were tabulated into Microsoft excel sheets and uploaded to Minitab version 13.0. The PCT and CRP was analyzed using ANOVA test. P-value of <0.05 was considered as statistically significant.

Results and Discussion

In this study Eighty (80) burned sequential patients were admitted to burn unit of hospitals for investigations, 30 (37.5%) patients were from the Imam Ali hospital and 50 (62.5%) from Al-Kindy hospital. Based on the clinical result, patients were divided into 24 (30%) non-survivor group and 56 (70%) survivor group. Our results declared that the mean of TBSA % affected were 63.5% range (36%–95%) in non-survivor, patients while 26.5% range (10% –70%) in survivor patients. There is a significant difference between two groups (P = 0.00) Figure 1 where, the higher mean percentage of TBSA has a significant association with mortality, but through recent years the progression in intensive care led to a significant reduction in mortality in burn injury patients. Many studies have demonstrated that TBSA% was a critical predictor of burn mortality [12-14].

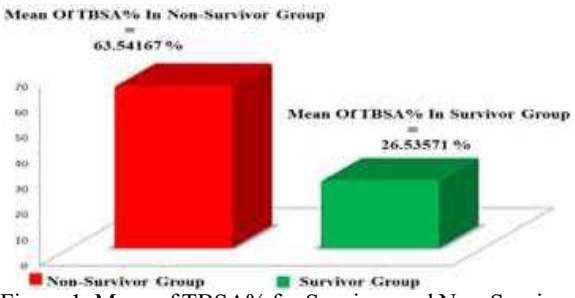

Figure 1: Mean of TBSA% for Survivor and Non-Survivor Groups as Predictor for Burn Mortality.

From the total of 80 burned patients, 50 were enrolled in the following tests in this study (15 non-survivors and 35 survivors), 30 patients were excluded from the study due to lack of blood sample adequacy. Serum PCT and CRP were measured three times, within the first 48hr

following admission, after 5th day and after 10th day, of admission where the averaged values of PCT concentrations have no significant differences (P>0.05) among the non-survivor group and within the survivor group of three times, but there were a strongly significant difference between survivor and non-survivor groups during 10th day time post-burn only (P=0.000).

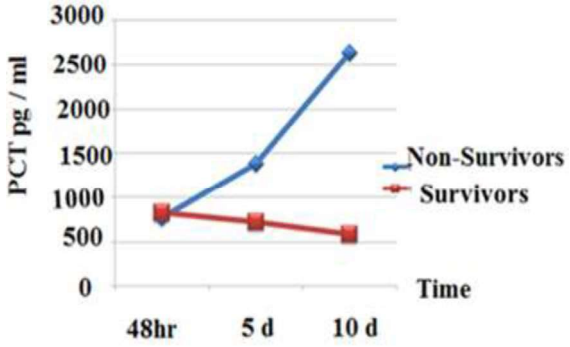

Figure 2: The PCT Concentration (pg/ml) in Correlation with Sampling Time in Survivor and None-Survivor Groups.

In other word the mean of PCT serum concentrations (2638 ± 3013 pg/ml) in non-survivor group were higher than the survivor group (588 ± 364 pg /ml). See Table 1, and Figure 2.

Our results showed no-normal distribution of Procalcitonin data in burn patients like other study in Table 2, perhaps there was another or mixed systemic infection like UTI, chest infections etc. Recently they found sometimes other conditions induce PCT (e.g. cardiogenic shock, major surgery including cardiac surgery, accidental trauma, pancreatitis, or burn trauma) [4][15][16].

Corresponds to the results of Rosnova *et al.*, 2015 [9], who found high PCT concentrations in dead patients. So did Castelli *et al*. [4] and Barati *et al.* [17] who indicated higher levels of PCT in burn injury patient with infections as compared to burn injury patients without infection.

Table 2: Mean of PCT Concentration (pg/ml) in Survivor and Non-Survivor Groups.

Group	No	Mean of PCT Concentration (Pg/ml)±SD			P value
		48hr	5th Day	10th Day	
Non-Survivor	15	773 ± 799	1383± 1972	2638 ± 3013	0.061
Survivor	35	827± 852	724± 573	588 ± 364	0.258
P value		P=0.837	P =0.074	P = 0.000**	

*P<0.05= Significant: **P<0.01= High Significant: P>0.05= Non Significant

Table 3: Differences in PCT Levels Between the Cases with Confirmed and Unconfirmed Infection.

Studies	Confirmed Infection	Unconfirmed infection	P value
Our study	2.638 ± 3.013	0.588 ±0.364	0.000
Von Heimburg *et al.*, 1998 [20]	49.8± 76.9	2.3 ±3.7	0.005
Lavrentieva *et al.*, 2007 [23]	11.5 ± 7.6	2.3 ± 3.7	0.05
Barati *et al.*, 2008 [17]	8.45± 7.8	0.5 ±1	0.001
Seoane *et al.* 2014 [18]	3.00± 5.43	0.56± 0.29	0.628
Mokline *et al.*, 2015 [8]	7.26 ± 7	0.9 ± 0.48	0.01

Table 4: CRP Concentration (mg/L) in Survivor and Non-Survivor Groups.

Group	No	Mean of PCT Concentration (Pg/ml)±SD			P value
		48hr	5th Day	10th Day	
Non-survivor	15	25.4 ± 32.45	38.6 ± 45.62	77.8 ± 58.26	0.01*
Survivor	35	20.6±26.1	32.97±28.48	19.46±20.36	0.05
P value		P= 0.582	P = 0.598	P = 0.000 **	

*P<0.05= Significant: **P<0.01= High Significant: P>0.05= Non Significant

Kim *et al.* [10] found that PCT levels could serve as a prognostic marker for burn patients and the concentrations ≥ 2 ng/ml provide a mortality marker. Secondary infection was a prevalent complication in burn injuries and late diagnosis is associated with increased morbidity, mortality, and also secondary infection lead to sepsis especially in burn injury patients and for these reasons, recognizing sepsis early is important. However, the systemic inflammation signs including changes in body temperature, tachycardia and leukocytosis are used for diagnosis of sepsis but sometimes can be misleading because critically ill burn patients often manifest a systemic inflammatory response syndrome without infection according to Mokline *et al.* [8].

Several studies suggested that PCT may not an accurate marker for sepsis in burn injured patients as a result of Rosanova *et al.*; Seoane *et al.* [9][18] in vice versa Mann *et al.* [19] concluded that PCT may be useful to diagnose sepsis in burn patients. Burn injury patients a general and complex example of the inflammatory process, including the inflammation mediators which lead to disruption of homeostasis and multiple organ failure.

Significantly high levels (mg/l) of C - reactive protein (CRP) were found between survivor and non-survivor groups especially in the 10^{th} day P=0. 000**.** Our results showed a significant differences within the non-survivor group and near to significant differences in survivor group through the three times P= 0.01**,** 0.05 respectively. See Table 4, and Figure 4.

C-reactive protein (CRP) known as acute-phase proteins whose consider as a biomarker for inflammatory response to infection, which indicating that CRP can be predictive of infection as found by Neely *et al.*, 1998 and Barati *et al.*, 2008 [21][17].

Our results were corresponds with Alkazaz *et al.,* 2014 and Jeschke *et al.*, 2013 [22][23] they found significantly increasing of CRP in burn injuries, but Lavrentieva *et al.*, 2007 [24], showed that serum CRP did not correlate with sepsis incidence while Neely *et al.*, 2004 [25] evaluated both CRP and PCT, and found that PCT did not correlate and predict sepsis, this disagreement continues related contradictory studies that investigated the effect of PCT and CRP as a biomarkers of severe infections after a burn injury like Barati *et al.*, 2008 and Sachse *et al.*, 1999 [17][26].

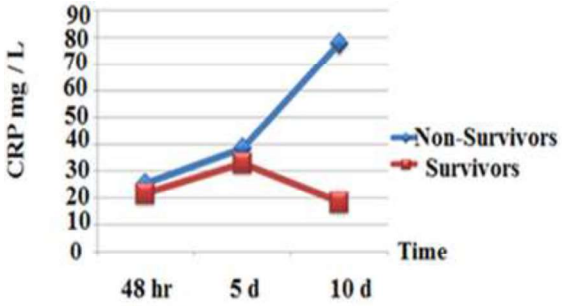

Figure 4: Comparison CRP Con. (mg/L) in Survivor and Non-Survivor Groups

CRP and PCT concentrations were analyzed according to the time after burn injury were significantly higher in dead patients as compared with survivor patients.

In this study, we have reached indicate that PCT and CRP both are infected-related parameters. However, both proteins are also induced by noninfectious causes of systemic inflammation and in patients with organ dysfunction. The PCT has demonstrated itself to be a parameter with a wide range of concentrations and clinically useful kinetics, thus being the better parameter of the two to estimate the severity, prognosis, and time course of the disease the result that conducted by Castelli *et al.* [4].

Conclusion

Our study demonstrates that TBSA is a critical predictor of burn mortality. C-reactive protein and procalcitonin are represent an early inflammatory indicator.

References

[1] Rowan, M. P.; Cancio, L. C.; Elster, E. A.; Burmeister, D. M.; Rose, L. F.; Natesan, S.and Chung, K. K. Burn wound healing and treatment: review and advancements. Critical care, 2015. 19, 243.

[2] Barret, J. P.; Herndon, D.N. Effects of burn wound excision on bacterial colonization and invasion. Plast Reconstr Surg 2003; 111 (2): 744-50; discussion 751-752.

[3] McCulloh, R.J. Biomarkers in Sepsis and Severe Infection: Where Immunology

Meets Diagnostics. 2012. J Immunodefic Disor 2012, 1: 1.

[4] Castelli, G.P.; Pognani, C.; Meisner, M.; Stuani, A., Bellomi, D. and Sgarbi, L. Procalcitonin and C-reactive protein during systemic inflammatory response syndrome, sepsis and organ dysfunction. Crit Care. 2004 Aug; 8 (4): R234-42.

[5] Aabenhus, R.[1]; Jensen, J.U. Procalcitoninguided antibiotic treatment of respiratory tract infections in a primary care setting: are we there yet? Prim Care Respir J. 2011 Dec, 20 (4): 360-7.

[6] Caliendo, A. M.[1]; Gilbert, D.N.; Ginocchio, C. C.; Hanson, K.E.; May, L.; Quinn, T.C.; Tenover, F.C.; Alland, D.; Blaschke, A.J.; Bonomo R.A., Carroll, K.C.; Ferraro, M.J.; Hirschhorn, L.R.; Joseph, W.P.; Karchmer T.; MacIntyre, A.T.; Reller, L.B. and Jackson, A.F. Infectious Diseases Society of America (IDSA). Better tests, better care: improved diagnostics for infectious diseases. Clin Infect Dis. 2013 Dec;57 Suppl 3: S139-70.

[7] Mohan, A. and Harikrishna, J. Biomarkers for the diagnosis of bacterial infections: in pursuit of the 'Holy Grail'Indian J Med Res. 2015 Mar; 141 (3): 271–273.

[8] Mokline, A.; Garsallah, L.;Rahmani, I.; Jerbi, K.; Oueslati, H.; Tlaili, S.; Hammouda, R.; Gasri, B.and Messadi, A.A. Procalcitonin: a diagnostic and prognostic biomarker of sepsis in burned patients. Ann Burns Fire Disasters. 2015 Jun 30;28 (2): 116-20.

[9] Rosanova, M. T.; Tramonti, N.; Taicz, M.; Martiren, S.; Basilico, H.; Signorelli, C.and Lede, R. Assessment of C-reactive protein and procalcitonin levels to predict infection and mortality in burn children. Arch Argent Pediatr, 2015. 113 (1), 36-41.

[10] Kim, H. S.; Yang, H. T.; Hur, J.; Chun, W.; Ju, Y. S.; Shin, S. H.and Lee, K. M. Procalcitonin levels within 48 hours after burn injury as a prognostic factor. Ann Clin Lab Sci, 2012. 42 (1), 57-64.

[11] Nakae, H.; Inaba, H.and Endo, S. Usefulness of procalcitonin in Pseudomonas burn wound sepsis model. Tohoku J Exp Med. 1999 Jul; 188 (3): 271-3.

[12] Tahir, S[1].; Memon, A.R.; Kumar, M.and Ali, S.A. Prediction of mortality after major burn: physiological versus biochemical measures. Wounds. 2009 Jul; 21 (7): 177-82.

[13] Zarei, M.R.[1]; Dianat, S.; Eslami, V.; Harirchi, I.; Boddouhi, N.; Zandieh A. and Rasouli, M.R. Factors associated with mortality in adult hospitalized burn patients in Tehran. Ulus Travma Acil Cerrahi Derg, 2011. Jan;17 (1): 61-5.

[14] Moore, E.C.; Pilcher, D.V.; Bailey, M.J.; Stephens, H.and Cleland, H. The Burns Evaluation and Mortality Study (BEAMS): predicting deaths in Australian and New Zealand burn patients admitted to intensive care with burns. Journal Trauma Acute Care Surg, 2013. Aug;75 (2): 298-303.

[15] Zhao, D.; Zhou, J.; Haraguchi, G.; Arai, H. and Mitaka, C.Procalcitonin for the differential diagnosis of infectious and non-infectious systemic inflammatory response syndrome after cardiac surgery. J Intensive Care, 2014. Jun 3;2: 35.

[16] Klingele, M.; Bomberg, H.; Poppleton, A.; Minko, P.; Speer, T.; Schäfers, H.J. and Groesdonk, H.V.Elevated procalcitonin in patients after cardiac surgery: a hint to nonocclusive mesenteric ischemia. Ann Thorac Surg, 2015. Apr;99 (4): 1306-12.

[17] Barati, M.; Alinejad, F.; Bahar, M. A.; Tabrisi, M. S.; Shamshiri, A. R. ;Bodouhi, N.O.; and Karimi, H. Comparison of WBC, ESR, CRP and PCT serum levels in septic and non-septic burn cases. Burns, 2008. 34 (6), 770-774.

[18] Seoane, L.; Pertega, S.; Galeiras, R.; Astola, I.; and Bouza, T. Procalcitonin in the burn unit and the diagnosis of infection. Burns, 2014. 40 (2), 223-229.

[19] Mann, E. A.; Wood, G. L.; and Wade, C. E. Use of procalcitonin for the detection of sepsis in the critically ill burn patient: a systematic review of the literature. Burns, 2011. 37 (4), 549-558.

[20] Von Heimburg, D., Stieghorst, W., Khorram-Sefat, R. and Pallua, N. Procalcitonin—a sepsis parameter in severe burn injuries. Burns, 1998. 24 (8), 745-750

[21] Neely, A. N.; Smith, W. L.; and Warden, G. D. Efficacy of a rise in C-reactive protein serum levels as an early indicator of sepsis in burned children. J Burn Care Rehabil, 1998. 19 (2), 102-105.

[22] Alkazaz F.F.; Abdulsattar S.A.; Farred F.A. and Mahmood S.J. Risk factor of metabolism alteration in burn patients. SENRA Academic Publishers, British Columbia, 2014.Vol. 8, No. 3, pp. 3057-3060,

[23] Jeschke, M. G.; Finnerty, C. C.; Kulp, G. A.; Kraft, R.; and Herndon, D. N. Can we use C-reactive protein levels to predict severe infection or sepsis in severely burned patients? International Journal of Burns and Trauma, 2013. 3 (3), 137-143.

[24] Lavrentieva, A.; Kontakiotis, T.; Lazaridis, L.; Tsotsolis, N.; Koumis, J.; Kyriazis, G.; and Bitzani, M. Inflammatory markers in patients with severe burn injury. What is the best indicator of sepsis? Burns, 2007. 33 (2), 189-194.

[25] Neely, A. N.; Fowler, L. A.; Kagan, R. J.; and Warden, G. D. Procalcitonin in pediatric burn patients: an early indicator of sepsis? Journal Burn Care Rehabil, 2004. 25 (1), 76-80.

[26] Sachse, C.; Machens, H. G.; Felmerer, G.; Berger, A.; and Henkel, E. Procalcitonin as a marker for the early diagnosis of severe infection after thermal injury. J Burn Care Rehabil, 1999. 20 (5), 354-360.